

CLAIMS

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1. A method of preventing, treating, or alleviating symptoms of any disease or clinical condition, which condition is at least partly the result of a defect in the cystic fibrosis transmembrane conductance regulator, the method comprising steps of:
identifying an individual at risk of or suffering from a condition that is at least partly the result of a defect in the cystic fibrosis transmembrane conductance regulator; and
administering a composition comprising at least two curcuminoids to the individual so that the disease or clinical condition is treated, prevented, or its symptoms relieved.
2. The method of claim 1, wherein the curcuminoids are selected from the group consisting of: curcumin, demethoxycurcumin, bisdemethoxycurcumin, and cyclocurcumin.
3. The method of claim 1, wherein at least one of the curcuminoids is curcumin.
4. The method of claim 1, wherein at least one of the curcuminoids is cyclocurcumin.
5. The method of claim 4, wherein the curcuminoids consist of at least 0.5% cyclocurcumin by weight.
6. The method of claim 4, wherein the curcuminoids consist of at least 1.0% cyclocurcumin by weight.
7. The method of claim 4, wherein the curcuminoids consist of at least 5.0% cyclocurcumin by weight.
8. The method of claim 4, wherein the curcuminoids consist of at least 10.0% cyclocurcumin by weight.

- 1 9. The method of claim 4, wherein the curcuminoids consist of at least 25.0%
2 cyclocurcumin by weight.
- 3 10. The method of claim 4, wherein the curcuminoids consist of at least 50.0%
4 cyclocurcumin by weight.
- 5 11. The method of claim 1, wherein at least one of the curcuminoids is curcumin.
- 6 12. The method of claim 1, wherein the condition is cystic fibrosis.
- 7 13. The method of claim 1, wherein the condition is rhinosinusitis.
- 8 14. The method of claim 1, further comprising the step of administering a curcumin
9 enhancing agent to the individual.
- 10 15. The method of claim 14, wherein the curcumin enhancing agent is included in the
11 composition.
- 12 16. The method of claim 1, wherein the curcumin enhancing agent is piperine.
- 13 17. The method of claim 1, wherein the curcumin enhancing agent is an inhibitor of a
14 curcumin metabolizing enzyme.
- 15 18. The method of claim 17, wherein the curcumin metabolizing enzyme is a cytochrome
16 P450.
- 17 19. The method of claim 1, wherein the composition, the agent, or both are administered
18 as an oral formulation.
- 19 20. The method of claim 1, wherein the composition, the agent, or both are administered
20 as an aerosolized or nebulized formulation.
- 21 21. The method of claim 1, wherein either the composition, the agent, or both are
22 administered intranasally.

- 1 22. The method of claim 1, wherein the composition comprises a curcumin related
2 compound.
- 3 23. The method of claim 1, wherein the composition comprises a 1,7-diaryl-1,6-
4 heptadiene-3,5-dione.
- 5 24. The method of claim 1, wherein the composition comprises a curcumin related
6 compound, analog, or derivative having an OH group at the 4 position of each phenyl
7 ring.
- 8 25. The method of claim 1, wherein the composition comprises curcumin or another
9 curcuminoid, curcumin related compound, curcumin analog, or curcumin derivative
10 synthesized *in vitro*.
- 11 26. The method of claim 1, wherein the composition decreases or inhibits activity of the
12 endoplasmic reticulum Ca^{++} ATPase.
- 13 27. The method of claim 1, wherein the composition lowers the concentration of Ca^{++}
14 within the ER.
- 15 28. The method of claim 1, wherein the composition causes release of proteins from the
16 endoplasmic reticulum.
- 17 29. The method of claim 1, wherein the composition causes release of mutant CFTR from
18 the endoplasmic reticulum.
- 19 30. The method of claim 29, wherein the mutant CFTR is ΔF508 CFTR.
- 20 31. A composition comprising:
21 (i) a first agent that increases CFTR functional activity; and
22 (ii) a second agent that causes increased release of CFTR from the ER,
23 wherein at least one of the agents is a curcuminoid.

- 1 32. The composition of claim 31, wherein the curcuminoid is selected from the group
2 consisting of: curcumin, demethoxycurcumin, bisdemethoxycurcumin, and
3 cyclocurcumin.
- 4 33. The composition of claim 32, wherein the curcuminoid is curcumin.
- 5 34. The composition of claim 32, wherein the curcuminoid is cyclocurcumin.
- 6 35. The composition of claim 31, wherein the first agent is selected from the group
7 consisting of: a flavone, an isoflavone, a benzimidazolone, a benzoquinolizinium, a
8 tetrahydrobenzothiophene, a benzofuran, a pyrimidinetrione, a dihydropyridine and an
9 anthraquinone.
- 10 36. The composition of claim 31, wherein the second agent is selected from the group
11 consisting of: thapsigargin, DBHQ, phenylbutyrate, and an anthracycline.
- 12 37. The composition of claim 31, further comprising a curcumin enhancing agent.
- 13 38. A method of preventing, treating, or alleviating symptoms of any disease or clinical
14 condition, which condition is at least partly the result of a defect in the cystic fibrosis
15 transmembrane conductance regulator, the method comprising steps of:
16 identifying an individual at risk of or suffering from a condition that is at least
17 partly the result of a defect in the cystic fibrosis transmembrane conductance
18 regulator; and
19 administering the composition of any of claims 31 to 37 to the individual.
- 20 39. A method of preventing, treating, or alleviating symptoms of any disease or clinical
21 condition, which condition is at least partly the result of a defect in the cystic fibrosis
22 transmembrane conductance regulator, the method comprising steps of:
23 identifying an individual at risk of or suffering from a condition that is at least
24 partly the result of a defect in the cystic fibrosis transmembrane conductance
25 regulator; and

- 1 administering a composition comprising at least one curcuminoid to the
 - 2 individual, wherein the curcuminoid activates the cystic fibrosis transmembrane
 - 3 conductance regulator, so that the disease or clinical condition is treated, prevented, or
 - 4 its symptoms relieved.
- 5 40. The method of claim 39, wherein the curcuminoid is cyclocurcumin.
 - 6 41. The method of claim 39, wherein the composition further comprises a curcumin
 - 7 enhancer.
 - 8 42. The method of claim 39, wherein the composition comprises an agent that increases
 - 9 release of the cystic fibrosis transmembrane conductance regulator from the endoplasmic
 - 10 reticulum.
 - 11 43. The method of claim 42, wherein the agent is selected from the group consisting of:
 - 12 thapsigargin, DBHQ, phenylbutyrate, and an anthracycline.
 - 13 44. The method of claim 39, wherein the condition is cystic fibrosis.
 - 14 45. The method of claim 39, wherein the condition is rhinosinusitis.
 - 15 46. The method of claim 39, wherein the cystic fibrosis transmembrane conductance
 - 16 regulator is a $\Delta F508$ mutant.
 - 17 47. A pharmaceutical composition comprising:
 - 18 (i) cyclocurcumin; and
 - 19 (ii) a pharmaceutically acceptable carrier.
 - 20 48. The pharmaceutical composition of claim 47, further comprising:
 - 21 a second curcuminoid, wherein at least 0.5% of total curcuminoids by weight
 - 22 is cyclocurcumin.
 - 23 49. The pharmaceutical composition of claim 48, wherein at least 1.0% of total
 - 24 curcuminoids by weight is cyclocurcumin.

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- 1 50. The pharmaceutical composition of claim 48, wherein at least 5.0% of total
2 curcuminoids by weight is cyclocurcumin.
- 3 51. The pharmaceutical composition of claim 48, wherein at least 10.0% of total
4 curcuminoids by weight is cyclocurcumin.
- 5 52. The pharmaceutical composition of claim 48, wherein at least 25.0% of total
6 curcuminoids by weight is cyclocurcumin.
- 7 53. The pharmaceutical composition of claim 48, wherein at least 50.0% of total
8 curcuminoids by weight is cyclocurcumin.
- 9 54. The pharmaceutical composition of claim 47 or claim 48, wherein the
10 pharmaceutically acceptable carrier is suitable for oral delivery.
- 11 55. The pharmaceutical composition of claim 47 or claim 48, further comprising a
12 curcumin enhancing agent.
- 13 56. The pharmaceutical composition of claim 47 or claim 48, wherein the composition is
14 nebulized or aerosolized.
- 15 57. A method of preventing, treating, or alleviating symptoms of any disease or clinical
16 condition, which condition is at least partly the result of a defect in the cystic fibrosis
17 transmembrane conductance regulator, the method comprising steps of:
18 identifying an individual at risk of or suffering from a condition that is at least
19 partly the result of a defect in the cystic fibrosis transmembrane conductance
20 regulator; and
21 administering the composition of any of claims 47 to 56, so that the disease or
22 clinical condition is treated, prevented, or its symptoms relieved.
- 23 58. A method of preventing, treating, or alleviating symptoms of any disease or clinical
24 condition, which condition is at least partly the result of a defect in the cystic fibrosis
25 transmembrane conductance regulator, the method comprising steps of:

1 identifying an individual at risk of or suffering from a condition that is at least
2 partly the result of a defect in the cystic fibrosis transmembrane conductance
3 regulator; and

4 administering to the individual a composition that causes improvement in at
5 least one sign or symptom of cystic fibrosis and results in an increased average
6 survival time.

7 59. A method of preventing, treating, or alleviating symptoms of any disease or clinical
8 condition, which condition is at least partly the result of a defect in the cystic fibrosis
9 transmembrane conductance regulator, the method comprising steps of:

10 identifying an individual at risk of or suffering from a condition that is at least
11 partly the result of a defect in the cystic fibrosis transmembrane conductance
12 regulator; and

13 administering to the individual a composition that causes normalization of
14 baseline sodium absorption.

15 60. The method of claim 58 or 59, wherein the cystic fibrosis transmembrane conductance
16 regulator is a $\Delta F508$ mutant.

17 61. The method of claim 58 or 59, wherein the composition comprises at least one
18 curcuminoid.

19 62. The method of claim 58 or 59, wherein the composition comprises curcumin.
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